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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,711	06/30/2000	Guy Serre	045636-5037	8393

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EXAMINER	
COOK, LISA V	
ART UNIT	PAPER NUMBER
1641	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/582,711	Applicant(s) SERRE ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 5-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group A (claims 1, 3, 5-12) drawn to compositions comprising sequence identification number 3(SEQ ID 3) in Paper No.14, filed 12/3/01 is acknowledged. The traversal on the ground(s) "that the peptides in the instant application all comprise the citrullinated tripeptide Ser-Cit-His therein the Ser-Cit-His is a common technical feature linking together peptides sequence identification 3, 5, and 6 (Paper #14, page 3, 3rd paragraph). This argument was carefully considered but is not found convincing.

This is not found persuasive because the cited sequences do not contain the Ser-Cit-His tripeptide motif. Also this common motif even if shared among the sequences would not totally impart patentability to each and every possible structure comprising the motif. Therein each sequence must be evaluated separately with respect to its total sequential information. Under PCT rules Applicant is entitled to an examination of one of the combination groupings: (1) a product and a method of using it – three different products have been claimed (seq. id. no.3, seq. id. No.5, and seq. id. No.6). Therein one sequence must be selected for consideration.

2. The Restriction Requirement is still deemed proper and is therefore made **FINAL.** Currently, claims 1, 3, and 5-12 with respect to sequence identification number 3 are pending and under examination.

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). The first line of the specification should reference priority applications PCT/FR98/02899 filed 29 December 1998 and foreign document FR 97 16,673 filed 30 December 1997. Please add to the specification.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

5. The information disclosure statements filed 6/30/00-Paper #7, has been considered as to the merits prior to first action. The information disclosure statement filed 6/30/00 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered. WO 98 08946 is a French publication an English translation is required.

Drawings

6. No drawings were filed in the instant application.

Specification

7. The use of several trademarks is noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. (For example, see page 12, lines 35-39 – NUNC, etc).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 3, and 5-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is directed to a peptide comprising a tripeptide motif Ser-Cit-His recognized by anti-flaggrin autoantibodies. However, applicants intended meaning with respect to this limitation is not clear. Since citrulline is an amino acid and not a peptide, the meaning of the expression "tripeptide unit" is not clear. Please explain.

B. In claims 8, The meaning of the expression "specifically present" is ambiguous as it could imply "only present on" and also "in particular, present on" which greatly modifies the scope of the claims. Appropriate correction is required.

9. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. There are no claimed steps reciting the washing or removal of unbound materials. If no separation will be performed it is unclear how the complex will be identified from the reaction solution containing both bound ad unbound material. Further, there are no steps that identify reagent and sample contact thereby forming a detectable complex which is correlated to the diagnosing and distinguishing of stroke as recited in the preamble.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 6 is rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The method has insufficient steps. These critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Merely, reciting the use of reagents in an assay format is not considered a proper method step.

An assay as recited in the preambles of claim 6, requires at least a contact step between reagent and sample – resulting in binding/complex formation, separation, detection, and a correlation step directed to the analysis of interest. The recited claims do not include the required steps for contact, detection, and correlation. Appropriate correction required.

11. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO: 3, 5, and 6, and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with a peptide molecule comprising particular tripeptide motif's centered on a citrulline residue of SEQ ID NO:3, 5, and 6 as recited in claim 8. The language of claim 8 suggests any amino acid on either side of the citrulline. Such variants are not described in the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Thomas E. Creighton, in his book, "Proteins: Structures and Molecular Properties, 1984, (pages 314-315) teaches that variation of the primary structure of a protein can result in an instable molecule. He also teaches a single amino acid change can cause a mutant.

Thus, the structure of the peptide of claim 8 is not defined. With the exception of SEQ ID NO:3, 5, and 6, the skilled artisan cannot envision the detailed structure of the encompassed compositions and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids/peptides by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus.

At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Further the disclosed sequences do not comprise the tripeptide motif and as such do not appear to encompass the instant invention.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Biomerieux et al. (FR 96/10651 filed 30 August 1996 – Derwent/Acc No. 1998-207042).

The invention relates to a flaggrin unit sequence comprising many X-Arg-Y units and in particular the Ser-Arg-His unit present on at least one of the sequences SEQ ID no. 3, 5, and 7. "This work resulted in the production of artificial antigens, which are recognized specifically by AFAs present in the serum from RA patients, and which consist of recombinant or synthetic polypeptides derived from the sequence of filaggrin or from portions of it, by substituting at least one arginine residue with a citrulline residue." On page 4, lines 24-38 of the specification applicant discloses the inventive concept in application FR 96/10651 filed 30 August 1996 in the name Biomerieux. Therefore it is not clear how the instant peptides differ from the ones taught by Biomerieux.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 7, 9-11, and 12 are rejected under 35 U.S.C.103(a) as being unpatentable over Serre et al.(U.S.Patent#5,888,833) in view of Biomerieux et al. (FR 96/10651 filed 30 August 1996– Derwent/Acc No. 1998-207042).

Serre et al. teach methods and kits to diagnosis rheumatoid arthritis via the contacting of an antigen to a biological sample to form an immune complex with autoantibodies as an indicator of RA. See claim 1 and 2, abstract, and column 1, lines 39-52.

The teachings of Serre et al. differ from the instant invention in not specifically teaching the peptide compositions or polypeptides derived from the sequence of filaggrin or from portions of it, by substituting at least one arginine residue with a citrulline residue.

However, The teachings of Biomerieux et al. (FR 96/10651 filed 30 August 1996) as set forth above disclose these compositions.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the peptide compositions as taught by Biomerieux et al. (FR 96/10651 filed 30 August 1996) and format them into an assay and kit to measure RA as in patent #5,888,833 of Serre et al. because Biomerieux et al. taught that the replacement of Arg by Cit was essential in antigen-specific recognition by the autoantibodies. See Derwent-Acc No. 1998-207042, advantage.

One having ordinary skill in the art would have been motivated to use the peptide compositions to detect RA because these antigens specifically recognized autoantibodies present in patients suffering from rheumatoid arthritis in respect of antigenic determinants in common with filaggrin and human profilaggrin. See abstract.

14. For reasons aforementioned, no claims are allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
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2/8/02

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800-1641